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YOUNG INVESTIGATOR AWARD

VITAMIN E MODIFICATION OF DAUNOMYCIN-INDUCED CARCINOGENESIS. Jim C. Kimball,* C.A. Gleiser,* Y-M Wang* (intr. by J.L. Simon), Departments of Pediatrics, Bowman Gray School of Medicine, Winston-Salem, North Carolina and M. D. Anderson Hospital, Houston, Texas.

Daunorubicin (DAU) is a known carcinogen in animals. The following study was undertaken to determine if Vitamin E (E) protects against DAU-induced mammary tumor formation. Three sets of 2 mo. old female rats were injected with 10, 12.5, or 15mg/kg DAU IV. Pretreatment with E (2.0gm/M^2) or 0.9% NaCl (equal volume) IP x 4d was administered to each group. Animals were sacrificed between 11 and 19 wks post DAU. Eight animals were used as NaCl controls. Erythroid and tissue glutathione (GSH) levels were determined by the DTNB method of Bleutler.

Erythroid GSH peaked 24 hrs after DAU in the NaCl set of rats while it reached a nadir in the E pretreated rats. Tissue GSH levels failed to demonstrate any trend relative to DAU, E, or NaCl. However, rats pretreated with E rarely developed tumors (1/16) while tumors developed in rats pretreated with NaCl (12/20). All tumors were adenocarcinomas. The appearance of mammary tumors appeared to be dose and time related. None of the 8 NaCl control rats developed tumors by 20 wks.

It has been previously reported that the antineoplastic effects of DAU are the result of DNA inhibition and that Vitamin E does not interfere with those effects. From the results of the present study, it would seem unlikely that the carcinogenicity of DAU is wholly dependent on DNA inhibition since E ameliorates the development of tumors. Rather, a reactive species, analogous to the generation of free radicals with resultant cardiotoxicity, would seem to be implicated in the carcinogenicity of the anthracyclines.

RECEPTORS FOR PEANUT AGGLUTININ (ARACHUS HYPOGEA) IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: POSSIBLE CLINICAL SIGNIFICANCE. E.C. Russell* T. Mohanakumar*, H.M. Maurer, Departments of Pediatrics and Surgery, Medical College of Virginia, Richmond, Virginia

Childhood acute lymphoblastic leukemia (ALL) is a protean disease which may be classified into T cell, B cell, null cell (non-T, non-B), and pre-B cell types on the basis of immunologic cell surface markers. This classification has prognostic significance but is incomplete in that many ALL patients have poor clinical courses despite the absence of T and B markers and the presence of favorable clinical and laboratory findings at diagnosis. Markers with greater specificity for the high risk patient would be useful in predicting subsequent clinical course and in treatment planning.

A direct immunofluorescence assay was used to detect the presence of receptors for the lectin peanut agglutinin (PNA) on blasts from 25 patients with ALL. Increased numbers (> 15%) of PNA+ cells were found in 3/4 T-ALL, 2/4 B-ALL and 8/17 null cell ALL patients. Only 6.1% of normal human peripheral blood lymphocytes were PNA+, while an average of 51% of fetal thymic lymphocytes expressed receptors for PNA. PNA binding was blocked specifically by the addition of galactose to the medium. No correlation was found between PNA positivity and any other clinical prognostic indicator. When all immunologic subgroups are combined, 13 patients had >15% PNA+ lymphoblasts and 8 of these have relapsed and subsequently died. None of the 12 patients with <15% PNA+ cells have relapsed. We conclude that analysis of PNA receptors on ALL lymphoblasts may be a useful adjunct to the existing clinical and immunological prognostic indicators.

EFFECT OF TRIIODOTHYRONINE ON THE METABOLISM OF VITAMIN D IN THE HYPOPHYSECTOMIZED MALE ALBINO RAT. A. Vargas,* and A. W. Root* (intr. by J.I. Malone), Department of Pediatrics, University of South Florida College of Medicine, Tampa, Florida.

The effects of triiodothyronine (T_3) upon the serum concentrations of 25OH vitamin D (25OHD) and $24,25(OH)_2$ vitamin D were investigated in male rats hypophysectomized (Hx) at 40 days of life. Intact control (IC) and Hx animals were grouped at 44 days of age: Group I (G1): IC fed ad lib, Group II (G2): pair fed IC, group III (G3): Hx, and Group IV (G4) Hx + T_3. G1, G3, G4 ate regular rat chow diet ad lib and G2 was pair fed to G3. Deionized water was supplemented with 0.9% NaCl and 5% sucrose to G3 and G4. T_3 in a diluent (0.9 µg/100 g body weight (BW)/day) was given for 20 days to G4 and just the diluent to G1, G2 and G3. Then the animals were decapitated. BW and tail length were greater in G1 ($p < 0.001$) and comparable in G2 and G4, the lowest in G3. Serum values were as follows:

		G1 (N)	G2	G3	G4
Ca	mg/dl	10 ±0.1(SE)(10)	7.8±0.2(15)	7.9±0.1(11)	7.7±0.1 (8)
PO_4	mg/dl	7.7±0.2(10)	6.8±0.2(14)	6.5±0.2(13)	7.2±0.2 (9)
25OHD	ng/ml	12.6±0.7(10)	12 ±0.4(14)	6.9±0.2(12)	14.4±0.7(10)
$24,25(OH)_2D$		3.2±0.1 (9)	3.2±0.2(14)	1.0±0.1(11)	1.8±0.2 (9)

Ca and PO_4 were higher ($p < 0.001$) in G1. 25OHD was significantly lower in G3 ($p < 0.001$) than in the other 3 groups. $24,25(OH)_2D$ was lower in G3 and G4 ($p < 0.001$) when compared to G1 and G2 and significantly lower in G3 ($p < 0.001$) when compared to G4. Conclusions: 1) Hypophysectomy lowers serum concentrations of 25OHD and $24,25(OH)_2D$, and this effect is independent of vitamin D intake; 2) T3 administration to Hx rats significantly increased $24,25(OH)_2D$ and 25OHD values suggesting thyroid hormones have a significant effect on vitamin D.

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